

WHAT IS CLAIMED IS:

1. Method for the production of recombinant DNA-derived heterologous protein in prokaryotic cells, wherein said heterologous protein is secreted extracellularly as an active and correctly folded protein, characterized in that the prokaryotic cell contains and expresses a vector comprising the DNA coding for said heterologous protein operably linked to the DNA coding for the signal peptide OmpA or a functional derivative thereof.

2. Method according to claim 1, characterised in that said the prokaryotic cell contains and expresses a vector comprising the DNA coding for said heterologous protein operably linked to the DNA coding for the signal peptide OmpA which is operably linked to the nucleic acid molecule defined by the sequence TCTGAGGGGAAACAGTGAC (SEQ ID NO:5) or a functional derivative thereof.

3. Method according to claim 1 or 2, characterised in that the prokaryotic cell is *E. coli*.

4. Method according to one of claims 1 to 3, characterised in that the the following steps are carried out:

a) the DNA encoding the heterologous protein is amplified by PCR;

b) the PCR product is purified;

c) said PCR product is inserted into a vector comprising the DNA coding for OmpA signal peptide and the DNA coding for gpIII in such a way that said PCR product is operably linked upstream to the DNA coding for the OmpA signal sequence and linked downstream to the DNA coding for gpIII of said vector;

d) that a stop codon is inserted between said heterologous protein and gpIII;

- e) said vector is expressed by the prokaryotic cell;
- f) the heterologous protein is purified.

5. Method according to one of claims 1 to 4, characterised in that the heterologous protein is selected from human tissue plasminogen activator or a fragment, a functional variant, an allelic variant, a subunit, a chemical derivative, a fusion protein or a glycosylation variant thereof.

6. Method according to one of claims 1 to 5, characterised in that the heterologous protein is selected from the K2S variant of human tissue plasminogen activator or a fragment, a functional variant, an allelic variant, a subunit, a chemical derivative, a fusion protein or a glycosylation variant thereof.

7. Method according to one of claims 1 to 6, characterised in that the vector is a phagemid vector comprising the DNA coding for OmpA signal peptide and the DNA coding for gpIII.

8. Method according to one of claims 1 to 7, characterised in that the vector is the pComb3HSS phagemid.

9. Method according to one of claims 1 to 8, characterised in that the DNA Sequence of OmpA comprises the following sequence:

ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCG
CTACCGTGGCCCAGGCGGCC (SEQ ID NO:1)

10. Method according to one of claims 1 to 9, characterised in that the DNA Sequence of OmpA consists of the following sequence:

ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCG
CTACCGTGGCCCAGGCGGCC (SEQ ID NO:1)

11. Method according to one of claims 1 to 10, characterised in that the DNA of the heterologous protein is preceded by a lac promotor and/or a ribosomal binding site.